Version With Markings to Show Changes Made

In the Specification:

Last paragraph of page 12 (lines 27-30):

Other suitable techniques (modified anti-solvent (GAS) techniques) [sinclude] include: Precipitation with Compressed Anti-Solvents (PCA) procedure (Dixon *et al., AIChE Journal*, **1993,** *39*, 127-139; and Supercritical Anti-Solvent (SAS) procedure (Yeo *et al., Biotech.Bioeng.*, **1993,** *41*, 341-346) or Aerosol Solvent Extraction System (ASES) (DE744329).

See pages 22, 23, 24 and 26 following:

In the Claims:

1. (Amended) A method for producing a vaccine delivery system comprising a plurality of polymer particles [for use as a vaccine delivery system in which], wherein a water insoluble protein antigen is incorporated with the polymer particles, the polymer particles comprising a [polymer] matrix polymer, wherein the method comprises:[-]

(a) mixing an aqueous phase (W) comprising the water insoluble protein and one or more solubilizing agents with an organic phase (O) that is immiscible with W to produce a W/O emulsion, [in which the water insoluble protein is solubilised in the W phase using a solubilizing agent, and] the O phase comprises the matrix polymer in an organic solvent;

(b) forming droplets of said W/O emulsion by dispersing the emulsion in a fluid medium, and removing said solvent from the O phase of the W/O emulsion droplets to thereby form the polymer particles incorporating the water insoluble protein antigen; and

wherein in step (a) [a stabilising agent is included] one or more stabilizing agents are provided in the W/O emulsion to stabilize the W/O emulsion in the presence of the solubilizing agent and promote the incorporation of the water insoluble protein with the polymer particles during step (b)[by stabilising the W/O emulsion in the presence of said solubilizing agent].

2. (Amended) The method of claim 1, wherein more than one [stabilising] stabilizing agent is included in the W/O emulsion.

3. (Amended) The method of claim 1 or 2, wherein the [or each stabilising] one or more stabilizing agents is/are selected from group consisting of polymers, polar lipids, and hydrophobic surfactants.

4. (Amended) The method of [any preceding] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] a polymer selected from the group consisting of poly(vinyl pyrrolidone), poly(vinyl alcohol), polysaccharides, polyethyleneoxide and water soluble proteins.

5. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents [is used that] is/are a polar lipid selected from the group consisting of cholesterol, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, glycolipids and phosphatidic acid.

6. (Amended) The method of[any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] a non-ionic, hydrophobic surfactant selected from the group consisting of a sorbitan fatty acid ester, hydrophobic polyoxyethylene alkyl ether, sucrose ester, alkyl-glucopyranoside, polyglycerol polyricinoleate and block-copolymers of ethylene oxide with propyleneoxide and/or lactic acid.

7. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] an anionic, hydrophobic surfactant selected from the group consisting of an alkylsulphate salt, a dialkylsulphosuccinate salt, an alkylbenzene sulphonate salt and a fatty acid salt.

8. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the stabilizing agent is/are [used that is] a cationic, hydrophobic surfactant selected from the group consisting of an alkyltrimethylammonium salt and a dialkyldimethylammonium salt.

9. (Amended) The method of claim 2, wherein one of the stabilizing agents is a sorbitan fatty acid ester[is used as a stabilising agent].

10. (Amended) The method of claim 2, wherein the stabilizing agents comprise poly(vinyl pyrrolidone) and sodium 1, 4-bis(2-ethylhexyl) sulphosuccinate[are used as stabilising agents].

11. (Amended) The method of [any preceding] claim 1, wherein the aqueous phase comprises more than one [solubilizing agent is used] solubilizing agent.

12. (Amended) The method of [any preceding] claim 1, wherein the one or more solubilizing agents is/are a hydrophilic surfactant[is used as a solubilizing agent].

13. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a non-ionic surfactant selected from the group consisting of alkyl-glucopyranosides, alkyl-thioglucopyranosides, alkyl-maltosides, alkoyl-methyl glucamides, glucamides, polyoxyethylene alcohols, polyoxyethylene alkyl phenols, emulphogens, polyoxyethylene sorbitol esters, polyoxyethylene fatty acid esters, hydrophilic polyoxyethylene alkyl ethers and digitonin.

14. (Amended) The method of claim 12, wherein the hydrophilic surfactant is an anionic surfactant selected from the group consisting of cholates, alkylsulphonates, deoxycholates, alkylsulphates, oligooxyethylene dodecyl ether sulphates and sodium dodecylsarcosinate.

15. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a cationic surfactant selected from the group consisting of alkylpyridinium salts and alkyltrimethylammonium salts.

16. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a zwitterionic surfactant selected from the group consisting of (3-[(3-cholamidopropyldimethylammonio]-1-propanesulphonate) (CHAPS), (3-[(3-cholamidopropyl)-dimethylammonio]-2-hydroxy-1-propanesulphonate) (CHAPSO), (N,N-*bis*[3-D-gluconamidopropyl]-cholamide) (BIGCHAP),

(N,N-bis[3-D-gluconamidopropyl]-deoxycholamide) (deoxy BIGCHAP), lyso phosphatidylcholine, alkylbetaines and sulphobetaines.

17. (Amended) The method of [any one of claims 1 to 11] claim 1, wherein the one or more solubilizing agents is/are a chaotropic agent[is used as a solubilizing agent].

18. (Amended) The method of claim 17, wherein the chaotropic agent is selected from the group consisting of a perchlorate, thiocyanate, guanidine, chlorate, iodide, bromide, nitrate and urea.

19. (Amended) The method of [any preceding] claim 1, wherein the method is a Double Emulsion (W/O/X) Solvent Evaporation Technique[for producing polymer particles for use as a vaccine delivery system, in which] and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets from which the solvent is evaporated[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

20. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein the method is a Double Emulsion (W/O/X) Solvent Extraction Technique[for producing polymer particles for use as a vaccine delivery system, in which] and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets, wherein the X phase extracts said solvent from the O phase of the droplets[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

21. (Amended) The [technique] method of claim 19 or 20, wherein [a stabilising agent is included in] the X phase comprises a stabilizing agent.

22. (Amended) The [technique] method of claim 21, wherein [a stabilising agent as defined in any one of claims 3 to 8 is used in the X phase] the one or more stabilizing agents is/are selected from group consisting of polymers, polar lipids, and hydrophobic surfactants.

23. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein the method is a spray drying technique [for producing polymer particles for use as a vaccine delivery system, in which], and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a gaseous medium to form a spray of W/O emulsion droplets from which said solvent evaporates[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

24. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein [in] step (b) comprises a fluid gas technique[is used] to form the polymer particles.

25. (Amended) The method of claim 24, wherein the fluid gas technique is selected from the group consisting of gas anti-solvent precipitation (GAS), solution enhanced dispersion by supercritical fluid (SEDS), precipitation with compressed anti-solvents (PCA), supercritical anti-solvent (SAS) and aerosol solvent extraction system (ASES).

26. (Amended) The method of [any preceding] claim 1, wherein the protein antigen is a *Helicobacter* protein or *Helicobacter* protein fragment[thereof].

27. (Amended) The method of claim 26, wherein the [protein antigen] *Helicobacter* protein or *Helicobacter* protein fragment [thereof] is from [a] *Helicobacter pylori* [protein or fragment thereof].

29. (Amended) The method of claim 28, wherein the *Helicobacter* protein is a lipidated form of *Helicobacter pylori* adhesion antigen (HpaA).

32. (Amended) The method of [any preceding] claim 1, wherein the matrix polymer is a homo-or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates, biodegradable polyurethanes, non-erodable polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

33. (Amended) The method of claim 32, wherein the matrix polymer is a polyester homopolymer selected from the group consisting of polylactic acid, polyglycolic acid, polyhydroxybutyrate, poly(alpha hydroxyacids) and polycaprolactone.

34. (Amended) The method of claim 32, wherein the matrix polymer is a polyester co-polymer selected from the group consisting of poly(lactide-co-glycolide), poly(lactic-co-glycolic acid), poly(hydroxybutyrate-hydroxyvalerate) and poly(lactide-co-caprolactone).

36. (Amended) The method of [any preceding] claim 1, wherein in step (a) the W phase is mixed with the O phase in a ratio by volume of 1:100 to 1:1.

37. (Amended) A [polymer particle] vaccine delivery system [obtainable] produced by the method of [any preceding] claim 1, wherein the one or more stabilizing agents is/are a polymer selected from the group consisting of poly(vinyl pyrrolidone), poly(vinyl alcohol), polysaccharides, polyethyleneoxide and water soluble proteins, and the method is a Double Emulsion (W/O/X) Solvent Evaporation Technique and in step (b) the stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets from which the solvent is evaporated.

38. (Amended) A [polymer particle]vaccine delivery system [in which] comprising a plurality of polymer particles, the polymer particles comprising a polymer matrix and a water insoluble protein antigen [is] incorporated with the polymer particles[comprising a polymer matrix].

45. (Amended) The vaccine delivery system of [any one of claims 38 to 44] claim 38, wherein the matrix polymer is a homo- or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates, biodegradable polyurethanes, non-erodable polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

46. (Amended) The vaccine delivery system of claim 45, wherein the polymer is a polyester homopolymer selected from the group consisting of polylactic acid, polyglycolic acid, polyhydroxybutyrate, poly(alpha hydroxyacids) and polycaprolactone.

47. (Amended) The vaccine delivery system of claim 45, wherein the matrix polymer is a polyester co-polymer selected from the group consisting of poly(lactide-co-glycolide), poly(lactic-co-glycolic acid), poly(hydroxybutyrate-hydroxyvalerate) and poly(lactide-co-caprolactone).

49. (Amended) The vaccine delivery system of any one of claims [37 to 48] 37, 38 and 45-48, wherein the polymer particles have an average diameter of 0.05-20 μm according to the volume size distribution.

50. (Amended) A vaccine composition comprising the vaccine delivery system of any one of claims [37 to 49] 37, 38, and 45-49.

51. (Amended) [Use of the delivery system of any one of claims 37 to 49 in the manufacture of a vaccine composition,] A method for the treatment of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 50.

52. (Amended) [Use of the delivery system of any one of claims 37 to 49 in the manufacture of a vaccine composition,] A method for preventing or reducing the risk of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 50.